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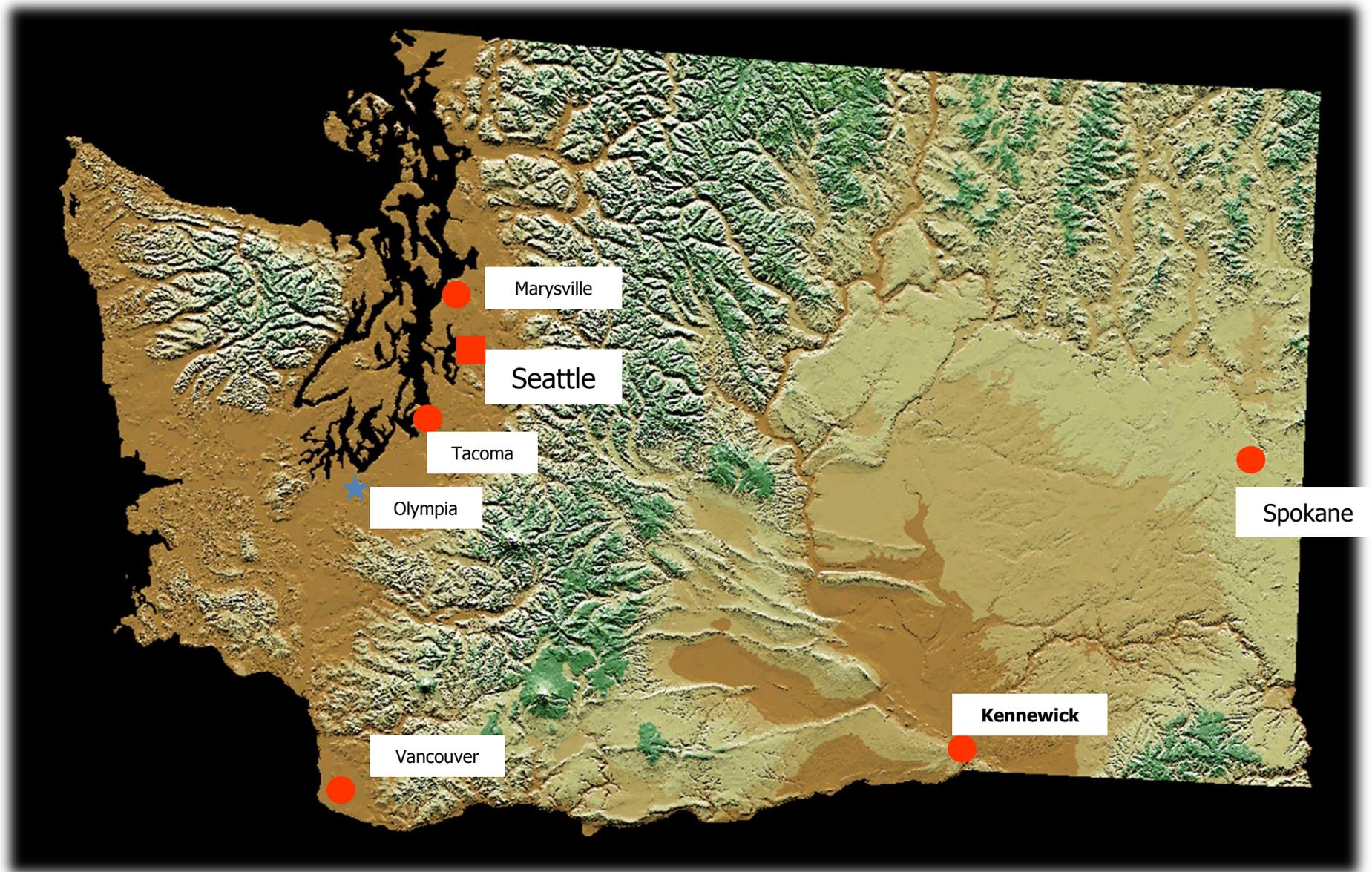
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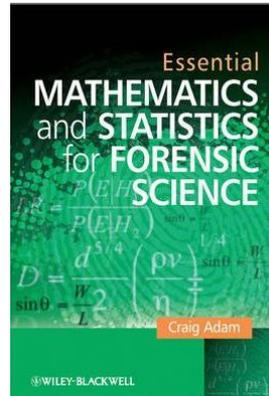
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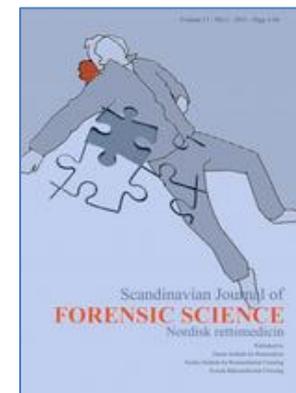
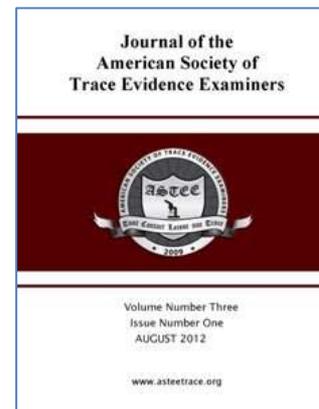
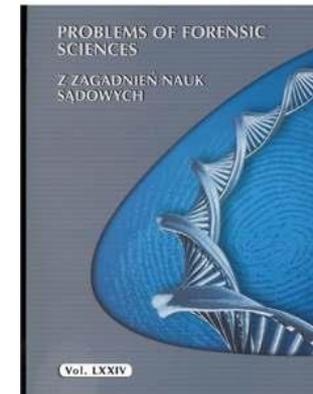
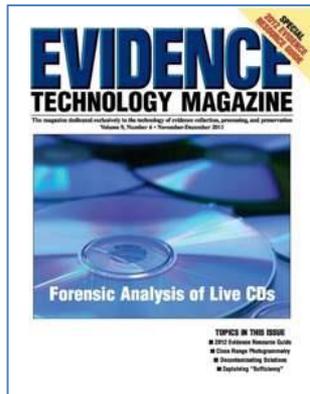


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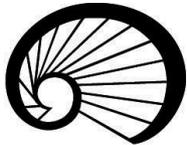
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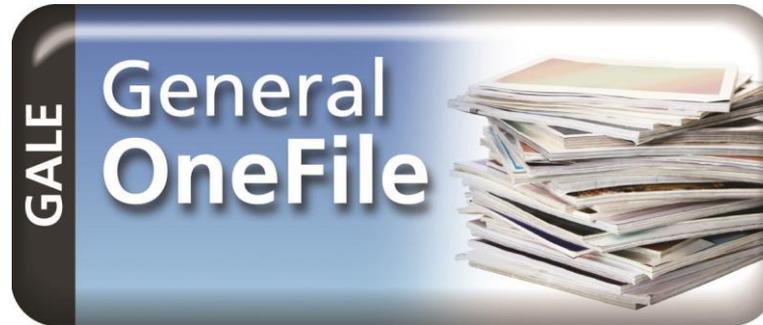
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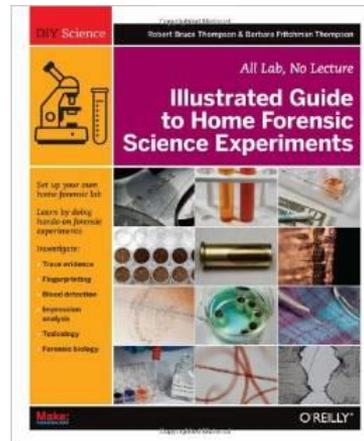
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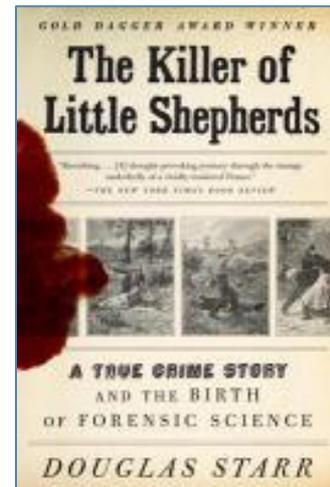
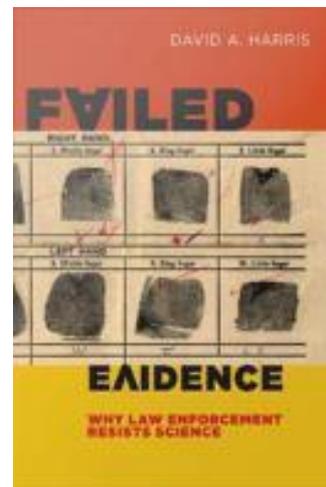
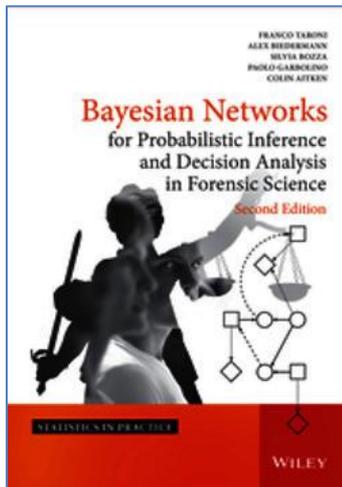
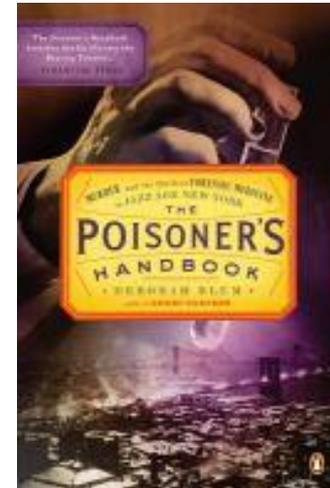
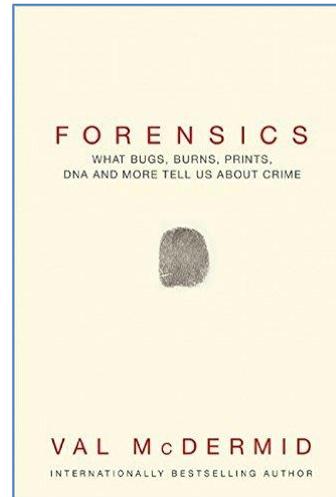
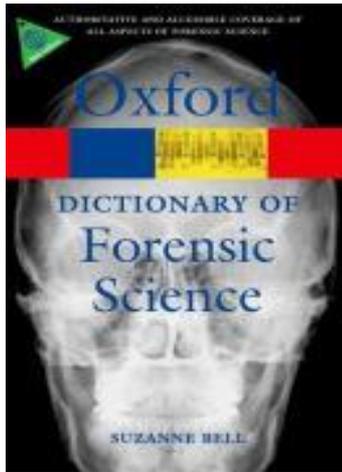


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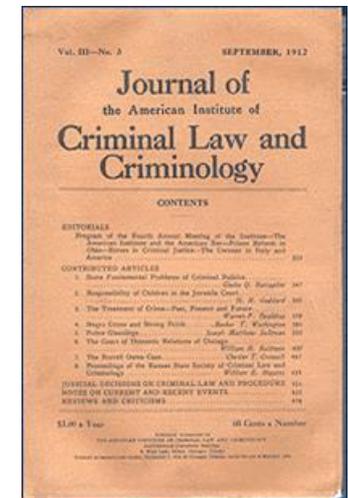
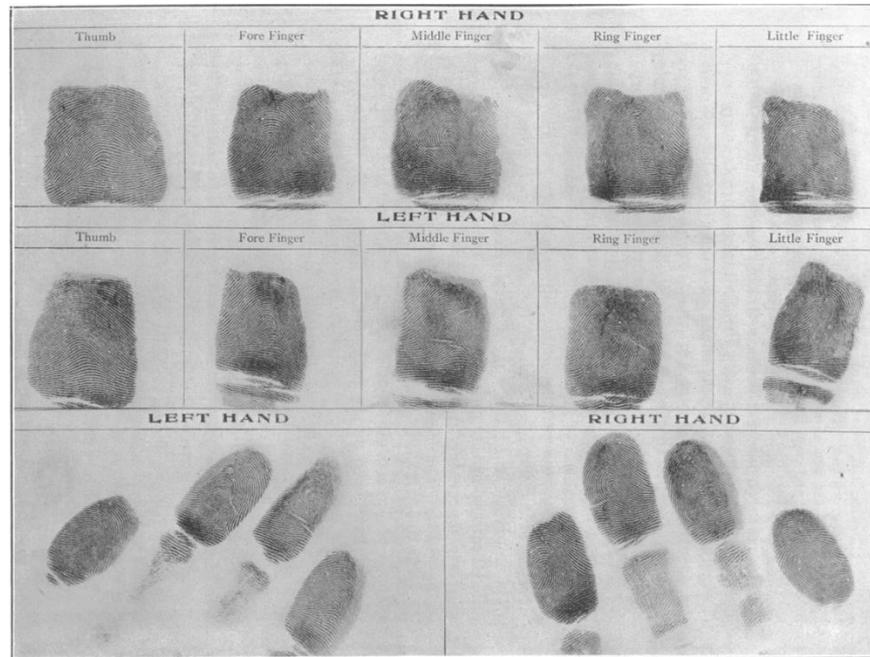


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Case report

## Death due to diabetic ketoacidosis: Induction by the consumption of synthetic cannabinoids



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### ARTICLE INFO

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Synthetic cannabinoids  
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Ketoacidosis

### ABSTRACT

We present a case study on a man who suffered from diabetic ketoacidosis, probably following consumption of synthetic cannabinoids. In blood from a femoral vein AB-CHMINACA, AB-FUBINACA, AM-2201, 5F-AMB, 5F-APINACA, EAM-2201, JWH-018, JWH-122, MAM-2201, STS135 and THJ 2201 could be detected by LC-MS/MS. Diagnosis of ketoacidosis as cause of death was carried out using biochemical measurements of glucose and lactate concentrations in vitreous humour (sum formula: 463 mg/dl) and cerebrospinal fluid (sum formula: 506 mg/dl), of acetone (163 mg/l in femoral venous blood) and of HbA1c (98 mmol/mol). Death due to hyperglycaemia could have been induced by skipping of insulin doses due to his intoxicated state or by the cannabinoids which were described to be able to produce hyperglycaemia themselves.

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### 1. Introduction

The internet drug market is flooded with steadily changing synthetic substances being consumed as an alternative to natural cannabis products. Synthetic cannabinoids have been shown to act as full agonists at CB<sub>1</sub> receptors with an increased affinity, thus leading to longer duration of effects and an increased likelihood of psychological effects. Those substances reach forensic interest because of possible serious intoxications mainly due to cardiac effects and can lead to death [1–4]. After the consumption of synthetic cannabinoids both symptoms which are also described after cannabis intoxications (tachycardia, sedation, psychosis, anxiety and panic attacks) and further symptoms like agitation, convulsions, nausea and emesis were detected [5,6]. In one case a patient suffered from chest pain after the use of K2 which ended in electrocardiogram changes (ST elevation), elevated troponin levels and myocardial infarction in a 16-year old [1]. Another patient died from sudden cardiac arrest after K2 consumption [3]. After the consumption of 5F-PB-22 (in combination with other drugs and alcohol) a young man suffered from severe coagulopathy, acute kidney injury, acute respiratory failure, hypoxaemia, severe anion gap metabolic and lactic acidosis. Cause of death was acute liver failure [2]. Gugelmann described a case of a generalized tonic-clonic seizure after the consumption of PB-22 [4].

Structures of synthetic cannabinoids detected in the presented case are shown in Fig. 1. Already published pharmacological potential of the substances described by their binding affinity and their activation potential of the human cannabinoid receptor types 1 and 2 are described in Table 1. 5F-AKB48 (5F-APINACA) and STS-135 (5F-APICA) are compounds with adamantyl moiety being sold on the internet market [7] and which could be detected in herbal mixtures and blood samples of cases with driving under the influence of drugs all over Europe [8–10]. UR-144, a substance with tetramethylcyclopropyl group selective for the CB<sub>2</sub> receptor was found in bulk material [11] and blood samples [8,12,13]. The synthetic cannabinoids JWH-122 and AM-2201 are well known substances synthesized in the beginning of the spice era [14,15]. MAM2201 and EAM2201 do only differ by the addition of a methyl (MAM2201) or ethyl (EAM2201) moiety in the 4-position of the naphthyl moiety from AM2201. Substances with 1-(aminocarbonyl)-2-methylpropyl] 3-carboxamide moiety are 5F-AMB, AB-FUBINACA and AB-CHMINACA.

Diabetic coma is the most severe form of hyperglycaemic metabolic disorders. The post mortem diagnosis of this disorder of glucose metabolism is difficult and vague due to a lack of characteristic morphological findings. Particularly biochemical measurements have to complement autopsy findings and case history in case of fatal hyperglycaemic dysregulations. Diabetic ketoacidosis is accompanied by high blood glucose levels and the presence of ketone bodies e.g. in blood. Blood glucose – at its maximum at the moment of death – is rapidly metabolized into lactate by glycolysis. Hence, it is not possible to draw important

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1. [The prevalence of new psychoactive substances in biological material - a three-year review of casework in Poland.](#)

Adamowicz P, Gieroń J, Gil D, Lechowicz W, Skulska A, Tokarczyk B.  
Drug Test Anal. 2015 Dec 14. doi: 10.1002/dta.1924. [Epub ahead of print] Review.  
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Swiss Med Wkly. 2015 Jan 14;145:w14043. doi: 10.4414/smw.2015.14043. eCollection 2015.

**Novel psychoactive substances (designer drugs): overview and pharmacology of modulators of monoamine signaling.**

[Liechti M](#)<sup>1</sup>.

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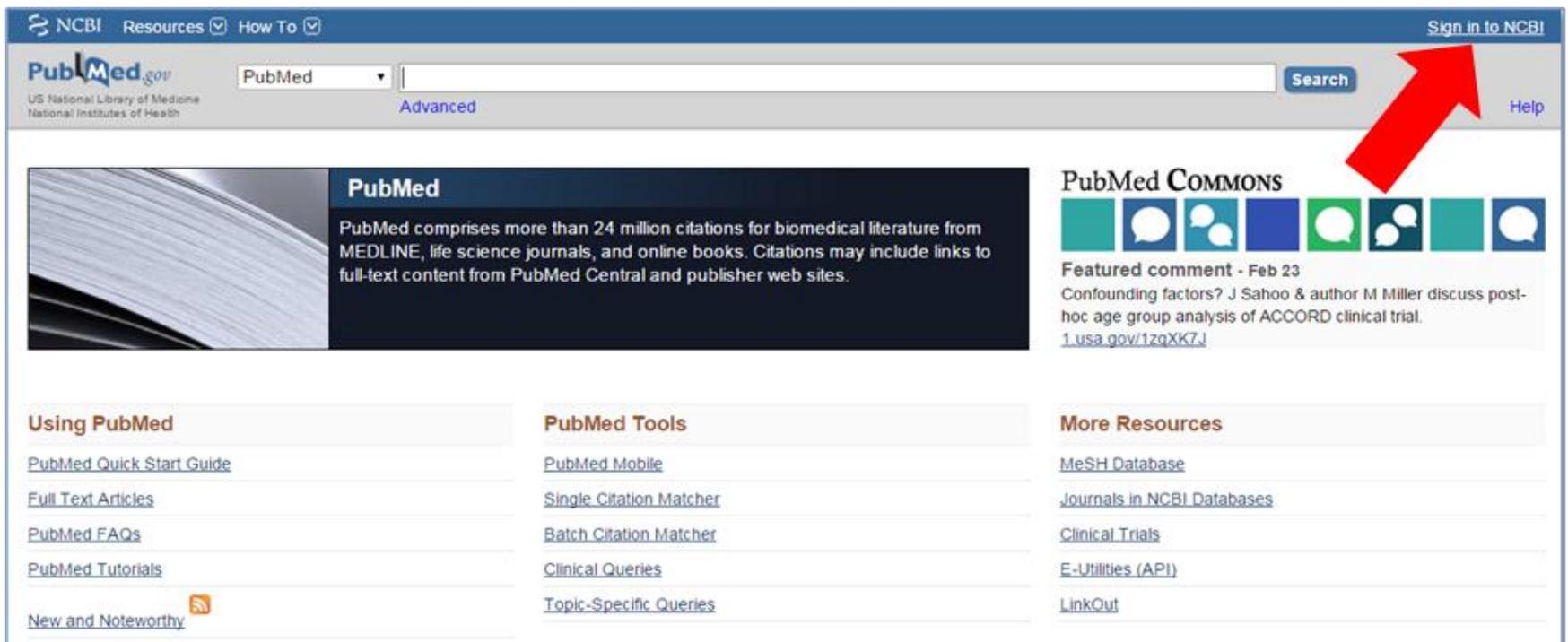


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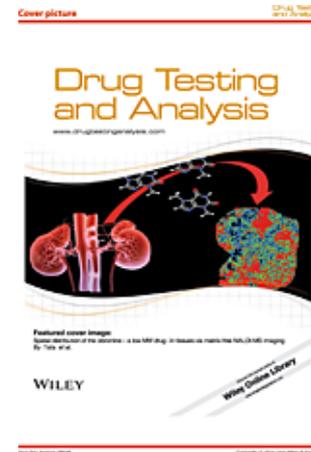
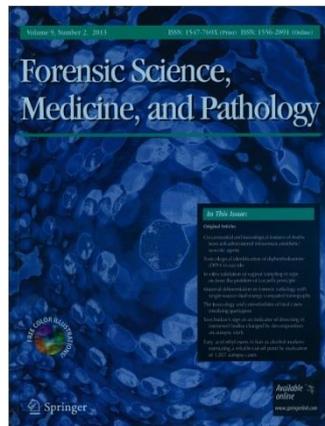
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## Novel psychoactive substances (NPS): clinical and pharmacological issues

Schifano, Fabrizio

□ [Drugs and Alcohol Today](#) , Volume 15 (1) – Mar 2, 2015

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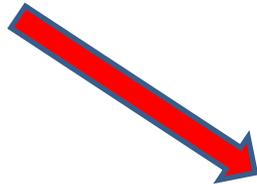
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## Novel psychoactive substances (NPS): clinical and pharmacological issues

Fabrizio Schifano

Professor Fabrizio Schifano is the Chair in Clinical Pharmacology, based at CRI Drug and Alcohol Recovery Services, Hatfield, UK and School of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK.

### Abstract

**Purpose** – The purpose of this paper is to provide health professionals with novel psychoactive substances (NPS) clients with up to date information relating to the background, clinical pharmacology and, where possible, clinical management for each of these categories.

**Design/methodology/approach** – The world of NPS is complex and diverse, including a range of different molecules such as: psychedelic phenethylamines; synthetic cannabinoids; cathinone derivatives; novel stimulants; synthetic catholopsichs; tryptamine derivatives; phenylcycidine-like dissociatives; piperazines; GABA-A/GABA-B receptor agonists; a range of prescribing medications; psychactive plants/herbs; and a large series of performance and image-enhancing drugs. These molecules are sought by users for their psychactive effects.

**Findings** – The NPS categorization and classification provided here is an attempt to identify and better understand some of these substances. Given the vast range of medical and psychopathological issues associated with the NPS described it is crucial for health professionals to be aware of the effects and toxicity of NPS. The EU-ADNESS project aims to both better understand the pharmacology of the available forthcoming NPS and to disseminate the most current NPS-related information to practising and training health professionals.

**Research limitations/implications** – Further studies are required to identify a range of evidence-based, NPS-focused, clinical management and treatment strategies.

**Social implications** – The rapid pace of change in the NPS online market constitutes a major challenge to the provision of current and reliable scientific knowledge on these substances.

**Originality/value** – The present review will provide an overview of the clinical and pharmacological issues related to a few hundred NPS.

**Keywords** Categories and classification, Clinical issues, Novel psychoactive substances, Pharmacological issues, Synthetic substances, Training for health professionals

**Paper type** Research paper

### Introduction

The present paper will provide an overview of the clinical and pharmacological issues related to a few hundred novel psychoactive substances (NPS; DeLuca *et al.*, 2012), grouped here for convenience in a range of categories (Schifano *et al.*, 2015), starting with the psychedelic phenethylamines' group (Schifano *et al.*, 2010; Schifano, 2011; Winstock and Schifano, 2009; Bersani *et al.*, 2014; Corazza *et al.*, 2011):

- in total, 179 "classical" PMA/phenethylamines/MDMA-like drugs; amphetamine-type substances (fluoroamphetamine, PMA, 2C-T, 2C-B, etc.);
- a dozen latest generation PIA derivatives; "Dromodrogenyl"; NDMs derivatives; indanes; benzofurans (e.g. APB/APOB; 5-EAPB; 5-MAPB; "Benzofury"); etc.; and
- in total, 125 psychedelic phenethylamines/stimulants from the Shugin Index (Shugin *et al.*, 2011); about 1,300 molecules being covered; including DMAA, etc.

MDMA/ecstasy misuse started at the end of the 1980s and steadily increased throughout the 1990s. The stimulant empathogenic (feelings of being closer to others) and entactogenic

The author is both a Core Member of the Advisory Council on the Misuse of Drugs (ACMD, UK) and a member of the Specialist Advisory Group (Psychiatry) for the European Medicines Agency (EMA).

No conflicts of interest are declared here that may have influenced the interpretation of the present data. The European Commission-funded EU-ADNESS project (2014-2016); contract no.: JUST/2013/ERP/ACU/48020 resources were used to assist with the preparation of this review.



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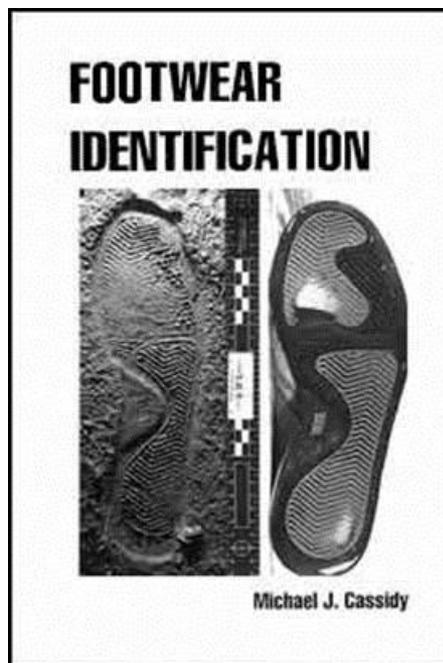
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